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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/536,804	WILLIAMSON ET AL.	
	Examiner	Art Unit	
	PETER J. REDDIG	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *76-114* is/are pending in the application.

4a) Of the above claim(s) *76-105 and 112-114* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *106-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 May 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/30/08; 5/27/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The response filed on January 30, 2008 to the restriction requirement of November 1, 2007 has been received. Applicant has elected Group 4, claims 106-111 and the species mutation site 5653 of the plexinB1 coding sequence and the A5653G mutation for examination. Because applicant did not distinctly and specifically point out any supposed errors in the restriction requirement, the election has been treated as an election without traverse MPEP 818.03(a).

2. Claims 76-114 are pending.

3. Claims 76-105 and 112-114 have also been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

4. Claims 106-111 as drawn to the elected species are currently under consideration.

Specification

5. The disclosure is objected to because of the following informalities: There are no heading for the various sections of the specification such as the Brief Description of the Drawings and the Background of the Invention.

Appropriate correction is required.

Drawings

6. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Figure 6 has the labels XF, XD, and XG on the x-axis and it is not clear to what these labels refer . Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in

reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 106-111 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: determining the expression of the plexinB1 nucleic acid in *a cell or a cell lysate* in the presence *of test compound*. The claims as written do not require clearly state of what the mutant plexinB1 nucleic acid is in the presence. Furthermore, the claims as written encompass contacting the mutant plexinB1 nucleic acid *in vitro* in the absence of any cellular components. Given that the expression of nucleic acids is controlled by the cellular transcription machinery in the cell, it is unclear how one would observe changes in the expression of the plexinB1 nucleic acid in the absence of these cellular transcription components.

8. Claims 107-109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 107 refers to one or more mutation in a region of the nucleic acid which encodes, the cytoplasmic domain of the plexinB1 polypeptide, Claim 108 refers to one or more mutations at site 5653 of the plexinB1 coding sequence and claim 109 refers to the mutation A5653G. However, given that there is no point of reference given as to where the cytoplasmic domain of plexinB1 begins or ends and there is no point of reference given as to where the mutations of claim 108 and 109 are located, such as a SEQ ID NO: for plexinB1, the claims are indefinite as it cannot be determined to where these mutations are located.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 106-111 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4)

the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claims are drawn to a method of identifying and/or obtaining a putative anti-cancer agent, the method comprising; contacting a plexinB1 nucleic acid with a test compound, wherein the plexinB1 nucleic acid comprises one or more mutations, and; determining the activity of the plexinB1 nucleic acid in the presence relative to the absence of test compound, wherein the mutation site of plexin B1 is 5653, and wherein the mutation is a A5653G mutation.

The specification teaches that PlexinB1 has been shown to interact with a variety of factors, including semaphorin 4D, c-Met, neuropilins, active Rac1 and the guanine nucleotide exchange factors (GEFS), PDZ-RhoGEF and LARG). The specification teaches that despite these interactions, the exact function of plexinB1 is not yet known, see para. 0004 of the published application.

The specification teaches that 80 primary prostate tumors and 11 prostate cancers metastases were screened for mutation in the cytoplasmic domain of plexinB1. The specification teaches that one of these mutations, A5653G, which potentially changes the threonine at position 1795 to an alanine, was found in 7/11 (64%) of metastases and 33/80 (41%) of primary cancers, see para 0258-0259 of the published application and Fig. 3i, Fig. 4, and Table 1.

The specification teaches that the transfection of a wild-type plexin B1 expression vector or the A5653G mutant expression vector into NIH-3T3 cells induced anchorage independent growth in these cells, although the anchorage independent growth with the A5653G mutant appeared to be less pronounced, See Figure 2.

The specification teaches that using these NIH-3T3 cells transfected with either the wild type or A5653G plexinB1 mutant in athymic nude mouse tumor studies, it was observed that the wild-type plexinB1 and the A5653G mutant reduced tumor formation compared to control transfected or parental cells. The specification teaches that however, the A5653G partially counteracted the reduction in tumor take rate observed with wild-type plexinB1, see para. 0267-0268 of the published application, and Figures 6 and 7.

One cannot extrapolate the teachings of the specification to the enablement of the claims because one of skill in the art would not be predictably able use changes in either the wild type plexinB1 or the A5653G mutant to identify or obtain a putative anti-cancer agent. Although the A5653G mutation is found in primary and metastatic prostate tumors, this same mutant plexinB1 reduces the tumorigenicity of cells *in vivo*. Thus, it is not clear if this mutation is a positive or negative regulator of prostate tumor or any tumor formation as the mutation appears to be associated with both positive and negative regulation of tumor formation and one of skill in the art would not predictably know what change in expression of the A5653G mutant B1 nucleic acid would be important for affecting tumor formation and would not predictably be able to identify and/or obtain a compound as a putative anti-cancer agent based on change in expression of the A5653G mutant plexin B1. Thus, undue experimentation would be required for identifying and/or obtaining a putative anti-cancer agent by the claimed method.

Additionally, it is not predictable that determining an increase in the wild-type plexinB1 would lead to the identification of a putative anti-cancer agent. Although the specification teaches that the expression of the wild-type plexin B1 suppresses tumor formation, Mack and Gish (US Pat. App. Pub. 2004/0005563, June 17, 2002) teach that plexin B1 is upregulated in

ovarian cancer, see Table 14A and para. 0348 of the published application and Vogelstein et al. (US Pat. App. Pub 2005/0047996, October 9, 2001) teach that plexin B1 is upregulated in colorectal cancer, see Table 1. Thus, given that plexin B1 is upregulated in ovarian and colorectal cancers, the determination of an increase in the wild-type plexin B1 by a test compound would not predictably identify a putative anti-cancer agent. Thus, undue experimentation would be required for identifying and/or obtaining a putative anti-cancer agent by the claimed method.

Furthermore, given that A5653G mutant plexin B1 has only be identified in prostate cancers, one of skill in the art would not predictable expect that agents that affect the expression of this mutant plexinB1 nucleic acid would be putative anti-cancer agents for any cancer because it is well known in the art that cancers are heterogenous in phenotype and genes expressed and cancer therapeutics are not predictably effective for all cancers.

In particular, cancers comprise a broad group of malignant neoplasms divided into two categories, carcinoma and sarcoma. The carcinomas originate in epithelial tissues while sarcomas develop from connective tissues, see Taber's Cyclopedic Medical Dictionary (1985, F.A. Davis Company, Philadelphia, p. 274). Given that not all cancers originate from the same tissue types, it is known that cancers originate from different tissue types have different structures as well as etiologies and would present differently. Thus, it would not be predictably expected that a nexus, for example drawn to a connection between the A5653G mutant plexin B1 and prostate cancer, would be established between two cancer types that arose from different tissue types. Further, it is well known that even two carcinomas that present on the same organ have significant differences in etiology and genetic constitution. For example, Busken, C et al,

(Digestive Disease Week Abstracts and Itinerary Planner, 2003, abstract No:850), teach that there is a difference in COX-2 expression with respect to intensity, homogeneity, localization and prognostic significance between adenocarcinoma of the cardia and distal esophagus, suggesting that these two cancers have different etiology and genetic constitution (last five lines of the abstract). Additionally, Kaiser (Science, 2006, 313, 1370) teaches that in a genomic analysis of mutations in breast and colon cancers, it was found that the cancer genes differ between each colon and breast cancers and each tumor had a different pattern of mutations. Kaiser teaches that the steps to cancer may be more complex than had been anticipated, see 3rd col. Furthermore, Krontiris and Capizzi (Internal Medicine, 4th Edition, Editor-in-chief Jay Stein, Elsevier Science, 1994 Chapters 71-72, pages 699-729) teach that the various types of cancers have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocols. Chemotherapeutic agents are frequently useful against a specific type of neoplasm and there are no drugs broadly effective against all forms of cancer, see Carter, S. K. et a1. Chemotherapy of Cancer; Second edition; John Wiley & Sons : New York, 1981; appendix C. Given the above, it is clear that it is not possible to predictably extrapolate any potential correlation between an A5653G mutant plexin B1 directed anti-cancer agents and prostate cancer sensitivity to such an agent in any tumor type based on the information in the specification and known in the art without undue experimentation.

Furthermore, one of skill in the art would not predictably expect that all of the broadly claimed mutants of plexinB1 to be associated with cancer and thus an effect on their expression would not predictably be useful for identifying a compound as a putative anti-cancer agent. It is noted that the specification teaches that a mutant plexinB1 nucleic acid may comprise a

nucleotide sequence which has one or more mutations relative to the wild-type plexinB1 nucleotide sequence, as set out in AB007867. The mutations may be deletions, insertions or substitutions of one or more nucleotides see para. 0014 of the published application. Given the above and given that claims are drawn to contacting "a" plexin B1 nucleic acid, which reads on fragments, which comprises one or more mutations in a coding region of the nucleic acid, the broadest reasonable interpretation of the claims is that the claims are not limited to any specific plexinB1 mutants and the plexinB1 mutants can comprise nucleic acids that are completely distinct from plexinB1. Furthermore, given claims 108 and 109 are indefinite in lacking a point of reference, these claims are also not limited to a particular site of mutation within the coding region of the plexinB1 nucleic acid and the plexinB1 mutants can comprise nucleic acids that are completely distinct from plexinB1.

It would not be expected that such a diverse array of mutants of plexin B1 would predictably be associated with cancer given that even naturally occurring gene variants, such as splice variants, do predictably have the same expression pattern or encode proteins with the same function as the related variants.. In particular, Benedict et al (J. Exp. Medicine, 2001, 193(1) 89-99) specifically teach that two splice isoforms of terminal deoxynucleotide transferase (a long form and a short form) enter the nucleus but have different activity, the long form does not catalyze nontemplated nucleotide addition but rather modulates the activity of the short form (see abstract). Jiang et al (JBC, 2003, 278(7) 4763-4769) specifically teach that the type 3 Ca2+ release channel, RyR3 exhibits strikingly different pharmacologic and functional properties depending on the tissues in which it resides. Upon examination, seven tissue specific alternatively spliced variants of

RyR3 were detected. One of the variants was unable to form a functional channel but was able to suppress the activity of a different release channel. The authors conclude that tissue-specific expression of RyR3 splice variants is likely to account for some of the pharmacologic and functional heterogeneities of RyR3 (see abstract). The abstract of Matsushita et al (FEBS Letters, 1999, Vol. 443, pp. 348-352) teaches that latrophilins exhibit alternative splicing resulting in latrophilin-1, which is present in brain and endocrine cells, latrophilin-2, which is ubiquitous, and latrophilin-3 which is brain-specific. The abstract of Singh et al (Glycobiology, 2001, Vol. 11, pp. 587-592) teaches that the CD44 splice variant, CD44v, is the major PNA-binding glycoprotein in colon cancer cells in contrast to standard CD44. These references serve to demonstrate that one of skill in the art cannot anticipate the biological activity of the proteins encoded by the broadly claimed plexinB1 mutants or the tissue distribution of the claimed mutants based on the biological activity of the protein encoded by the wild-type or tissue distribution of the wild-type nucleic acid or other mutants of plexinB1. Thus, even if it were found that the examination of the expression of the A5653G plexin B1 mutant could be used as claimed, undue experimentation would be required to use the broadly claimed mutants or even other mutations at position 5653 for the identification of putative anti-cancer agents.

The specification provides insufficient guidance with regard to the issues set forth above and provides insufficient working examples which would provide guidance to one skilled in the art and insufficient evidence has been provided which would allow one of skill in the art to predict that the invention would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would

be required to practice the claimed invention.

10. Claims 106-111 are rejected as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of identifying and/or obtaining a putative anti-cancer agent, the method comprising; contacting a plexinB1 nucleic acid with a test compound, wherein the plexinB1 nucleic acid comprises one or more mutations, and; determining the activity of the plexinB1 nucleic acid in the presence relative to the absence of test compound, wherein the mutation site of plexin B1 is 5653, and wherein the mutation site of plexin B1 is A5653G. When given the broadest reasonable interpretation, a plexinB1 nucleic acid which comprises one or more mutations encompasses any nucleic acid, given that the specification teaches, as set forth above, the mutations may be deletions, insertions or substitutions of one or more nucleotides. Thus, the genus of plexinB1 nucleic acids which comprise one or more mutations is highly variant which vary significantly both in structure and function from each other. The description of plexin B1 mutations (see Table 1 and 2) in the specification fails to adequately describe the genus of plexin B1 mutations because said genus tolerates members which differ significantly in both structure and function from the plexinB1 nucleic acid. One of skill in the art can reasonably conclude that applicant was not in possession of a genus of plexinB1 nucleic acids which comprise one or more mutations at the time the invention was filed. Because the genus of plexinB1 nucleic acids which comprise one or more mutations is not adequately described, the method claims relying on said genus are also not adequately described.

As it is drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

In the instant case the genus of plexinB1 nucleic acids which comprise one or more mutations is so broad that it does not define the members that do or do not fall with the genus and it does not define any structural features commonly possessed by members of the genus that

distinguish them from nucleic acids not encompassed by the genus. Although claims 108 and 109 point to the site of mutation as 5653 of the plexinB1 coding sequence or A5653G, no point of reference is given for the location of these sites that would distinguish these sites so that it can be determined where these mutation lie within the plexinB1 sequence or even if they lie with a plexinB1 related sequence. Thus, claims 108 and 109 are still drawn to a large genus of sequences of structurally distinct nucleic acids and do not define any structural features commonly possessed by members of the genus that distinguish them from nucleic acids not encompassed by the genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 106-111 are rejected under 35 U.S.C. 102(b) as being anticipated by Tang et al. (WO 01/54477, 2 August 2001, IDS).

The claims are drawn to:

106. A method of identifying and/or obtaining a compound as a putative anti-cancer agent, the method comprising; contacting a plexinB1 nucleic acid with a test compound, wherein the plexinB1 nucleic acid comprises one or more mutations in a coding region of the nucleic acid, and; determining the expression of the plexinB1 nucleic acid in the

presence relative to the absence of test compound.

107. A method according to claim 106, wherein the one or more mutations are in a region of the nucleic acid which encodes the cytoplasmic domain of the plexinB1 polypeptide.

108. A method according to claim 107, wherein the one or more mutations are at 5653 of the plexinB1 coding sequence.

109. A method according to claim 107, wherein the one or more mutations are A5653G.

110. A method according to claim 106, further comprising determining the increase in the expression of wild-type plexin B1 in the presence of said test compound.

111. A method according to claim 106, comprising determining a decrease in the expression of mutant plexin B1 in the presence of said test compound

It is noted that the specification teaches that mutant plexinB1 nucleic acid may comprise a nucleotide sequence which has one or more mutations relative to the wild-type plexinB1 nucleotide sequence, as set out in AB007867. The mutations may be deletions, insertions or substitutions of one or more nucleotides. The one or more mutations may be in a coding or non-coding region of the plexin nucleic acid sequence and may alter the expression or function of the plexinB1 polypeptide. In other words, the mutant nucleic acid may encode a mutant plexinB1 polypeptide sequence with aberrant activity, or may encode a wild-type plexinB1 polypeptide which is expressed at an aberrant e.g. an increased or reduced, level, for example by means of an alteration in the activity of a plexinB1 regulatory element. A mutant nucleic acid may have one, two, three, four or more mutations relative to the wild-type sequence, see para. 0014 of the published application.

Given the above and given that claims are drawn to contacting "a" plexin B1 nucleic acid, which reads on fragments, which comprises one or more mutations in a coding region of the nucleic acid, the broadest reasonable interpretation of the claims is that the claims are not limited to any specific plexinB1 mutants and the plexinB1 mutants can comprise nucleic acids that are completely distinct from plexinB1. Furthermore, given claims 107-109 are indefinite in lacking a point of reference, these claims are also not limited to a particular site of mutation within the coding region of the plexinB1 nucleic acid and the plexinB1 mutants can comprise nucleic acids that are completely distinct from plexinB1.

Tang et al. teach the plexin B1 nucleic acid, see Table 2. Tang et al. teach that polynucleotides of the invention include nucleotide variants with variations in the coding sequence, see p. 3, lines 10-23 and p. 7-8 and 14-18. Tang et al. teach methods for the identification of compounds that increase or decrease the expression of the polynucleotides of the invention, see p. 5, lines 19-21. Tang et al. teach antisense RNA and ribozymes for inhibiting the expression of the polynucleotides of the invention, see p. 20-24.

Given the broadly claimed mutant plexinB1 nucleotides and given that Tang et al. teach measuring increases and decreases in plexinB1 polynucleotide expression and variant polynucleotides in compound identification and using antisense RNA and ribozymes, although the reference does not specifically state that methods were for identifying and/or obtaining a compound as a putative anti-cancer agent, the claimed method will inherently be a method for identifying and/or obtaining a compound as a putative anti-cancer agent, given that the art teaches the same method steps, See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

12. Claims 106-111 are rejected under 35 U.S.C. 102(e) as being anticipated by Mack and Gish (US Pat. App. Pub. 2004/0005563, June 17, 2002).

The claims are drawn to:

106. A method of identifying and/or obtaining a compound as a putative anti-cancer agent, the method comprising; contacting a plexinB1 nucleic acid with a test compound, wherein the plexinB1 nucleic acid comprises one or more mutations in a coding region of the nucleic acid, and; determining the expression of the plexinB1 nucleic acid in the presence relative to the absence of test compound.

107. A method according to claim 106, wherein the one or more mutations are in a region of the nucleic acid which encodes the cytoplasmic domain of the plexinB1 polypeptide.

108. A method according to claim 107, wherein the one or more mutations are at 5653 of the plexinB1 coding sequence.

109. A method according to claim 107, wherein the one or more mutations are A5653G.

110. A method according to claim 106, further comprising determining the increase in the expression of wild-type plexin B1 in the presence of said test compound.

111. A method according to claim 106, comprising determining a decrease in the expression of mutant plexin B1 in the presence of said test compound

It is noted that the specification teaches that mutant plexinB1 nucleic acid may comprise a nucleotide sequence which has one or more mutations relative to the wild-type plexinB1 nucleotide sequence, as set out in AB007867. The mutations may be deletions, insertions or substitutions of one or more nucleotides. The one or more mutations may be in a coding or non-coding region of the plexin nucleic acid sequence and may alter the expression or function of the

plexinB1 polypeptide. In other words, the mutant nucleic acid may encode a mutant plexinB1 polypeptide sequence with aberrant activity, or may encode a wild-type plexinB1 polypeptide which is expressed at an aberrant e.g. an increased or reduced, level, for example by means of an alteration in the activity of a plexinB1 regulatory element. A mutant nucleic acid may have one, two, three, four or more mutations relative to the wild-type sequence, see para. 0014 of the published application.

Given the above and given that claims are drawn to contacting "a" plexin B1 nucleic acid, which reads on fragments, which comprises one or more mutations in a coding region of the nucleic acid, the broadest reasonable interpretation of the claims is that the claims are not limited to any specific plexinB1 mutants and the plexinB1 mutants can comprise nucleic acids that are completely distinct from plexinB1. Furthermore, given claims 107-109 are indefinite in lacking a point of reference, these claims are also not limited to a particular site of mutation within the coding region of the plexinB1 nucleic acid and the plexinB1 mutants can comprise nucleic acids that are completely distinct from plexinB1.

Mack and Gish (US Pat. App. Pub. 2004/0005563, June 18, 2001) teach that plexinB1 nucleic acid is upregulated in ovarian cancer, see Table 14A and para. 0348 of the published application. Mack and Gish teach an ovarian drug screening assay of administering a test compound to a mammal having ovarian cancer or to a cell sample isolated from; (ii) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1-20 in a treated cell or mammal with the level of gene expression of the polynucleotide in a control cell sample or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the

treatment of ovarian cancer. Mack and Gish teach that the method of screening drug candidates includes comparing the level of expression in the absence of the drug candidate to the level of expression in the presence of the drug candidate, wherein the concentration of the drug candidate can vary when present, and wherein the comparison can occur after addition or removal of the drug candidate. Mack and Gish teach that the genes may show an increase or decrease see para. 0040-0048.

Mack and Gish teach assaying for activators and inhibitors of ovarian cancer, including inhibitory or antisense nucleic acids that bind directly to the coding regions of the nucleic acids of the invention by measurement of changes in mRNA level, see para 0093-0095. Mack and Gish teach antisense RNA, siRNA, and ribozymes for inhibiting the expression of the polynucleotides of the invention, see para 0307-0316.

Given the broadly claimed mutant plexinB1 nucleotides claimed and given that Mack and Gish teach measuring nucleotides that are at least 80% identical to plexin B1 and measuring increases and decreases in these polynucleotides in ovarian drug screening assays, Mack and Gish anticipate the claimed method.

Information Disclosure Statement

13. The information disclosure statement filed May 27, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Electronic versions of the documents were considered by the Examiner, but Applicants are required to submit copies of the cited references per 37 CFR 1.98(a)(2) to make the record complete.

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PETER J. REDDIG whose telephone number is (571)272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Helms Larry can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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